

SEQUENCE LISTING

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<120> Methods for Modulating FXR Receptor
Activity

<130> 17302

<140> 09/590,447

<141> 2000-06-09

<150> 60/138,986

<151> 1999-06-11

<160> 10

<170> FastSEQ for Windows Version 3.0

<210> 1

<211> 469

<212> PRT

<213> Rattus norvegicus

<400> 1

Met	Asn	Leu	Ile	Gly	Pro	Ser	His	Leu	Gln	Ala	Thr	Asp	Glu	Phe	Ala
1				5					10					15	
Leu	Ser	Glu	Asn	Leu	Phe	Gly	Val	Leu	Thr	Glu	His	Ala	Ala	Gly	Pro
			20					25					30		
Leu	Gly	Gln	Asn	Leu	Asp	Leu	Glu	Ser	Tyr	Ser	Pro	Tyr	Asn	Asn	Val
		35					40					45			
Gln	Phe	Pro	Gln	Val	Gln	Pro	Gln	Ile	Ser	Ser	Ser	Ser	Tyr	Tyr	Ser
	50					55				60					
Asn	Leu	Gly	Phe	Tyr	Pro	Gln	Gln	Pro	Glu	Asp	Trp	Tyr	Ser	Pro	Gly
65					70				75					80	
Leu	Tyr	Glu	Leu	Arg	Arg	Met	Pro	Thr	Glu	Ser	Val	Tyr	Gln	Gly	Glu
			85					90					95		
Thr	Glu	Val	Ser	Glu	Met	Pro	Val	Thr	Lys	Lys	Pro	Arg	Met	Ala	Ala
		100						105					110		
Ser	Ser	Ala	Gly	Arg	Ile	Lys	Gly	Asp	Glu	Leu	Cys	Val	Val	Cys	Gly
		115				120					125				
Asp	Arg	Ala	Ser	Gly	Tyr	His	Tyr	Asn	Ala	Leu	Thr	Cys	Glu	Gly	Cys
	130					135					140				
Lys	Gly	Phe	Phe	Arg	Arg	Ser	Ile	Thr	Lys	Asn	Ala	Val	Tyr	Lys	Cys
145					150					155				160	
Lys	Asn	Gly	Gly	Asn	Cys	Val	Met	Asp	Met	Tyr	Met	Arg	Arg	Lys	Cys
			165					170						175	
Gln	Asp	Cys	Arg	Leu	Arg	Lys	Cys	Arg	Glu	Met	Gly	Met	Leu	Ala	Glu
		180						185					190		
Cys	Leu	Leu	Thr	Glu	Ile	Gln	Cys	Lys	Ser	Lys	Arg	Leu	Arg	Lys	Asn
		195					200					205			
Val	Lys	Gln	His	Ala	Asp	Gln	Thr	Val	Asn	Glu	Asp	Ser	Glu	Gly	Arg
	210					215					220				
Asp	Leu	Arg	Gln	Val	Thr	Ser	Thr	Thr	Lys	Leu	Cys	Arg	Glu	Lys	Thr

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225 230 235 240
 Glu Leu Thr Val Asp Gln Gln Thr Leu Leu Asp Tyr Ile Met Asp Ser
 245 250 255
 Tyr Ser Lys Gln Arg Met Pro Gln Glu Ile Thr Asn Lys Ile Leu Lys
 260 265 270
 Glu Glu Phe Ser Ala Glu Glu Asn Phe Leu Ile Leu Thr Glu Met Ala
 275 280 285
 Thr Ser His Val Gln Ile Leu Val Glu Phe Thr Lys Arg Leu Pro Gly
 290 295 300
 Phe Gln Thr Leu Asp His Glu Asp Gln Ile Ala Leu Leu Lys Gly Ser
 305 310 315 320
 Ala Val Glu Ala Met Phe Leu Arg Ser Ala Glu Ile Phe Asn Lys Lys
 325 330 335
 Leu Pro Ala Gly His Ala Asp Leu Leu Glu Glu Arg Ile Arg Lys Ser
 340 345 350
 Gly Ile Ser Asp Glu Tyr Ile Thr Pro Met Phe Ser Phe Tyr Lys Ser
 355 360 365
 Val Gly Glu Leu Lys Met Thr Gln Glu Glu Tyr Ala Leu Leu Thr Ala
 370 375 380
 Ile Val Ile Leu Ser Pro Asp Arg Gln Tyr Ile Lys Asp Arg Glu Ala
 385 390 395 400
 Val Glu Lys Leu Gln Glu Pro Leu Leu Asp Val Leu Gln Lys Leu Cys
 405 410 415
 Lys Ile Tyr Gln Pro Glu Asn Pro Gln His Phe Ala Cys Leu Leu Gly
 420 425 430
 Arg Leu Thr Glu Leu Arg Thr Phe Asn His His His Ala Glu Met Leu
 435 440 445
 Met Ser Trp Arg Val Asn Asp His Lys Phe Thr Pro Leu Leu Cys Glu
 450 455 460
 Ile Trp Asp Val Gln
 465

<210> 2

<211> 484

<212> PRT

<213> Mus musculus

<400> 2

Met Val Met Gln Phe Gln Gly Leu Glu Asn Pro Ile Gln Ile Ser Leu
 1 5 10 15
 His His Ser His Arg Leu Ser Gly Phe Val Pro Asp Gly Met Ser Val
 20 25 30
 Lys Pro Ala Lys Gly Met Leu Thr Glu His Ala Ala Gly Pro Leu Gly
 35 40 45
 Gln Asn Leu Asp Leu Glu Ser Tyr Ser Pro Tyr Asn Asn Val Pro Phe
 50 55 60
 Pro Gln Val Gln Pro Gln Ile Ser Ser Ser Ser Tyr Tyr Ser Asn Leu
 65 70 75 80
 Gly Phe Tyr Pro Gln Gln Pro Glu Asp Trp Tyr Ser Pro Gly Ile Tyr
 85 90 95
 Glu Leu Arg Arg Met Pro Ala Glu Thr Gly Tyr Gln Gly Glu Thr Glu
 100 105 110
 Val Ser Glu Met Pro Val Thr Lys Lys Pro Arg Met Ala Ala Ala Ser
 115 120 125
 Ala Gly Arg Ile Lys Gly Asp Glu Leu Cys Val Val Cys Gly Asp Arg
 130 135 140
 Ala Ser Gly Tyr His Tyr Asn Ala Leu Thr Cys Glu Gly Cys Lys Gly

145 150 155 160
 Phe Phe Arg Arg Ser Ile Thr Lys Asn Ala Val Tyr Lys Cys Lys Asn
 165 170 175
 Gly Gly Asn Cys Val Met Asp Met Tyr Met Arg Arg Lys Cys Gln Glu
 180 185 190
 Cys Arg Leu Arg Lys Cys Arg Glu Met Gly Met Leu Ala Glu Cys Leu
 195 200 205
 Leu Thr Glu Ile Gln Cys Lys Ser Lys Arg Leu Arg Lys Asn Val Lys
 210 215 220
 Gln His Ala Asp Gln Thr Val Asn Glu Asp Asp Ser Glu Gly Arg Asp
 225 230 235 240
 Leu Arg Gln Val Thr Ser Thr Thr Lys Phe Cys Arg Glu Lys Thr Glu
 245 250 255
 Leu Thr Ala Asp Gln Gln Thr Leu Leu Asp Tyr Ile Met Asp Ser Tyr
 260 265 270
 Asn Lys Gln Arg Met Pro Gln Glu Ile Thr Asn Lys Ile Leu Lys Glu
 275 280 285
 Glu Phe Ser Ala Glu Glu Asn Phe Leu Ile Leu Thr Glu Met Ala Thr
 290 295 300
 Ser His Val Gln Ile Leu Val Glu Phe Thr Lys Lys Leu Pro Gly Phe
 305 310 315 320
 Gln Thr Leu Asp His Glu Asp Gln Ile Ala Leu Leu Lys Gly Ser Ala
 325 330 335
 Val Glu Ala Met Phe Leu Arg Ser Ala Glu Ile Phe Asn Lys Lys Leu
 340 345 350
 Pro Ala Gly His Ala Asp Leu Leu Glu Glu Arg Ile Arg Lys Ser Gly
 355 360 365
 Ile Ser Asp Glu Tyr Ile Thr Pro Met Phe Ser Phe Tyr Lys Ser Val
 370 375 380
 Gly Glu Leu Lys Met Thr Gln Glu Glu Tyr Ala Leu Leu Thr Ala Ile
 385 390 395 400
 Val Ile Leu Ser Pro Asp Arg Gln Tyr Ile Lys Asp Arg Glu Ala Val
 405 410 415
 Glu Lys Leu Gln Glu Pro Leu Leu Asp Val Leu Gln Lys Leu Cys Lys
 420 425 430
 Met Tyr Gln Pro Glu Asn Pro Gln His Phe Ala Cys Leu Leu Gly Arg
 435 440 445
 Leu Thr Glu Leu Arg Thr Phe Asn His His His Ala Glu Met Leu Met
 450 455 460
 Ser Trp Arg Val Asn Asp His Lys Phe Thr Pro Leu Leu Cys Glu Ile
 465 470 475 480
 Trp Asp Val Gln

<210> 3

<211> 472

<212> PRT

<213> Homo sapiens

<400> 3

Met Gly Ser Lys Met Asn Leu Ile Glu His Ser His Leu Pro Thr Thr
 1 5 10 15
 Asp Glu Phe Ser Phe Ser Glu Asn Leu Phe Gly Val Leu Thr Glu Gln
 20 25 30
 Val Ala Gly Pro Leu Gly Gln Asn Leu Glu Val Glu Pro Tyr Ser Gln
 35 40 45
 Tyr Ser Asn Val Gln Phe Pro Gln Val Gln Pro Gln Ile Ser Ser Ser

B'cont.

50	55	60
Ser Tyr Tyr Ser Asn Leu Gly Phe Tyr Pro Gln Gln Pro Glu Glu Trp		
65	70	75
Tyr Ser Pro Gly Ile Tyr Glu Leu Arg Arg Met Pro Ala Glu Thr Leu		80
	85	90
Tyr Gln Gly Glu Thr Glu Val Ala Glu Met Pro Val Thr Lys Lys Pro		95
	100	105
Arg Met Gly Ala Ser Ala Gly Arg Ile Lys Gly Asp Glu Leu Cys Val		110
	115	120
Val Cys Gly Asp Arg Ala Ser Gly Tyr His Tyr Asn Ala Leu Thr Cys		125
	130	135
Glu Gly Cys Lys Gly Phe Arg Arg Ser Ile Thr Lys Asn Ala Val		140
145	150	155
Tyr Lys Cys Lys Asn Gly Gly Asn Cys Val Met Asp Met Tyr Met Arg		160
	165	170
Arg Lys Cys Gln Glu Cys Arg Leu Arg Lys Cys Lys Glu Met Gly Met		175
	180	185
Leu Ala Glu Cys Leu Leu Thr Glu Ile Gln Cys Lys Ser Lys Arg Leu		190
	195	200
Arg Lys Asn Val Lys Gln His Ala Asp Gln Thr Val Asn Glu Asp Ser		205
	210	215
Glu Gly Arg Asp Leu Arg Gln Val Thr Ser Thr Thr Lys Ser Cys Arg		220
225	230	235
Glu Lys Thr Glu Leu Thr Pro Asp Gln Gln Thr Leu Leu His Phe Ile		240
	245	250
Met Asp Ser Tyr Asn Lys Gln Arg Met Pro Gln Glu Ile Thr Asn Lys		255
	260	265
Ile Leu Lys Glu Glu Phe Ser Ala Glu Glu Asn Phe Leu Ile Leu Thr		270
	275	280
Glu Met Ala Thr Asn His Val Gln Val Leu Val Glu Phe Thr Lys Lys		285
	290	295
Leu Pro Gly Phe Gln Thr Leu Asp His Glu Asp Gln Ile Ala Leu Leu		300
305	310	315
Lys Gly Ser Ala Val Glu Ala Met Phe Leu Arg Ser Ala Glu Ile Phe		320
	325	330
Asn Lys Lys Leu Pro Ser Gly His Ser Asp Leu Leu Glu Glu Arg Ile		335
	340	345
Arg Asn Ser Gly Ile Ser Asp Glu Tyr Ile Thr Pro Met Phe Ser Phe		350
	355	360
Tyr Lys Ser Ile Gly Glu Leu Lys Met Thr Gln Glu Glu Tyr Ala Leu		365
	370	375
Leu Thr Ala Ile Val Ile Leu Ser Pro Asp Arg Gln Tyr Ile Lys Asp		380
385	390	395
Arg Glu Ala Val Glu Lys Leu Gln Glu Pro Leu Leu Asp Val Leu Gln		400
	405	410
Lys Leu Cys Lys Ile His Gln Pro Glu Asn Pro Gln His Phe Ala Cys		415
	420	425
Leu Leu Gly Arg Leu Thr Glu Leu Arg Thr Phe Asn His His His Ala		430
	435	440
Glu Met Leu Met Ser Trp Arg Val Asn Asp His Lys Phe Thr Pro Leu		445
	450	455
Leu Cys Glu Ile Trp Asp Val Gln		460
465	470	

<210> 4

<211> 462

<212> PRT

<213> Homo sapiens

<400> 4

Met Asp Thr Lys His Phe Leu Pro Leu Asp Phe Ser Thr Gln Val Asn
1 5 10 15
Ser Ser Leu Thr Ser Pro Thr Gly Arg Gly Ser Met Ala Ala Pro Ser
20 25 30
Leu His Pro Ser Leu Gly Pro Gly Ile Gly Ser Pro Gly Gln Leu His
35 40 45
Ser Pro Ile Ser Thr Leu Ser Ser Pro Ile Asn Gly Met Gly Pro Pro
50 55 60
Phe Ser Val Ile Ser Ser Pro Met Gly Pro His Ser Met Ser Val Pro
65 70 75 80
Thr Thr Pro Thr Leu Gly Phe Ser Thr Gly Ser Pro Gln Leu Ser Ser
85 90 95
Pro Met Asn Pro Val Ser Ser Ser Glu Asp Ile Lys Pro Pro Leu Gly
100 105 110
Leu Asn Gly Val Leu Lys Val Pro Ala His Pro Ser Gly Asn Met Ala
115 120 125
Ser Phe Thr Lys His Ile Cys Ala Ile Cys Gly Asp Arg Ser Ser Gly
130 135 140
Lys His Tyr Gly Val Tyr Ser Cys Glu Gly Cys Lys Gly Phe Phe Lys
145 150 155 160
Arg Thr Val Arg Lys Asp Leu Thr Tyr Thr Cys Arg Asp Asn Lys Asp
165 170 175
Cys Leu Ile Asp Lys Arg Gln Arg Asn Arg Cys Gln Tyr Cys Arg Tyr
180 185 190
Gln Lys Cys Leu Ala Met Gly Met Lys Arg Glu Ala Val Gln Glu Glu
195 200 205
Arg Gln Arg Gly Lys Asp Arg Asn Glu Asn Glu Val Glu Ser Thr Ser
210 215 220
Ser Ala Asn Glu Asp Met Pro Val Glu Arg Ile Leu Glu Ala Glu Leu
225 230 235 240
Ala Val Glu Pro Lys Thr Glu Thr Tyr Val Glu Ala Asn Met Gly Leu
245 250 255
Asn Pro Ser Ser Pro Asn Asp Pro Val Thr Asn Ile Cys Gln Ala Ala
260 265 270
Asp Lys Gln Leu Phe Thr Leu Val Glu Trp Ala Lys Arg Ile Pro His
275 280 285
Phe Ser Glu Leu Pro Leu Asp Asp Gln Val Ile Leu Leu Arg Ala Gly
290 295 300
Trp Asn Glu Leu Leu Ile Ala Ser Phe Ser His Arg Ser Ile Ala Val
305 310 315 320
Lys Asp Gly Ile Leu Leu Ala Thr Gly Leu His Val His Arg Asn Ser
325 330 335
Ala His Ser Ala Gly Val Gly Ala Ile Phe Asp Arg Val Leu Thr Glu
340 345 350
Leu Val Ser Lys Met Arg Asp Met Gln Met Asp Lys Thr Glu Leu Gly
355 360 365
Cys Leu Arg Ala Ile Val Leu Phe Asn Pro Asp Ser Lys Gly Leu Ser
370 375 380
Asn Pro Ala Glu Val Glu Ala Leu Arg Glu Lys Val Tyr Ala Ser Leu
385 390 395 400
Glu Ala Tyr Cys Lys His Lys Tyr Pro Glu Gln Pro Gly Arg Phe Ala
405 410 415
Lys Leu Leu Leu Arg Leu Pro Ala Leu Arg Ser Ile Gly Leu Lys Cys
420 425 430

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Leu Glu His Leu Phe Phe Phe Lys Leu Ile Gly Asp Thr Pro Ile Asp
 435 440 445
 Thr Phe Leu Met Glu Met Leu Glu Ala Pro His Gln Met Thr
 450 455 460

<210> 5

<211> 147

<212> PRT

<213> Saccharomyces cerevisiae

<400> 5

Met Lys Leu Leu Ser Ser Ile Glu Gln Ala Cys Asp Ile Cys Arg Leu
 1 5 10 15
 Lys Lys Leu Lys Cys Ser Lys Glu Lys Pro Lys Cys Ala Lys Cys Leu
 20 25 30
 Lys Asn Asn Trp Glu Cys Arg Tyr Ser Pro Lys Thr Lys Arg Ser Pro
 35 40 45
 Leu Thr Arg Ala His Leu Thr Glu Val Glu Ser Arg Leu Glu Arg Leu
 50 55 60
 Glu Gln Leu Phe Leu Leu Ile Phe Pro Arg Glu Asp Leu Asp Met Ile
 65 70 75 80
 Leu Lys Met Asp Ser Leu Gln Asp Ile Lys Ala Leu Leu Thr Gly Leu
 85 90 95
 Phe Val Gln Asp Asn Val Asn Lys Asp Ala Val Thr Asp Arg Leu Ala
 100 105 110
 Ser Val Glu Thr Asp Met Pro Leu Thr Leu Arg Gln His Arg Ile Ser
 115 120 125
 Ala Thr Ser Ser Ser Glu Glu Ser Ser Asn Lys Gly Gln Arg Gln Leu
 130 135 140
 Thr Val Ser
 145

<210> 6

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> Junction between yeast GAL-4 DBD and human RXR
 alpha LBD coding regions in GAL-L-RXR

<400> 6

gtatcgccgg aattcggtac cgctcaggcc gtgcaggag

39

<210> 7

<211> 56

<212> DNA

<213> Artificial Sequence

<220>

<223> Junction between yeast GAL-4 DBD and rat RXR alpha
 LBD coding regions in GAL-L-RXR

<400> 7

gtatcgccgg aattcgggct aaggaagtgc agagagatgg gaatgttggc tgaatg

56

<210> 8

P cont.

<211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> SV40 nuclear localization sequence

<400> 8
 Ala Pro Lys Lys Lys Arg Lys Val Gly
 1 5

<210> 9
 <211> 360
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Promoter region of plasmid TK-luc

<400> 9
 gggttttccca gtcacgacgt tgtaaaacga cggccagtgc caagcttgca tgccctgcagg 60
 tcgactctag aggatccggc cccgcccagc gtcttgatcat tggcgaattc gaacacgcag 120
 atgcagtcgg ggcggcgcg tcccaggtcc acttcgcata ttaaggtgac gcgtgtggcc 180
 tcgaacaccg agcgaccctg cagcgacccg cttaacagcg tcaacagcgt gccgcagatc 240
 tctcgagtcc ggtactgttg gtaaaatgga agacgccaaa aacataaaga aaggcccggc 300
 gccattctat cctctagagg atggaaccgc tggagagcaa ctgcataagg ctatgaagag 360

<210> 10
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Consensus S. cerevisiae UAGg response element

<400> 10
 cgacggagta ctgtcctccg agct 24